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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LEFFERS JR, GERALD G	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 07/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/720,252	HELIBRONN, REGINE	
	Examiner	Art Unit	
	Gerald G Leffers Jr., PhD	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-60* is/are pending in the application.

4a) Of the above claim(s) *60* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of a supplemental response filed 4/9/2004 in response to a request mailed by the examiner on 3/31/2004 for a new amendment where all of the pending claims are cancelled and re-presented as new claims in order to clarify the record. Accordingly, claims 1-31 have been cancelled and new claims 32-60 have been submitted in the response filed 4/9/2004.

New claim 60 appears to correspond to nonelected Group VI (claim 28) and has therefore been withdrawn from consideration for reasons of record in the action mailed 11/22/2002 as Paper No. 11. Claims 32-60 are pending, with claim 60 withdrawn from consideration as being directed to a nonelected invention.

Receipt is also acknowledged of a response filed 2/24/2003 in which arguments were made concerning the rejections of record in the office action mailed on 11/22/2002 as Paper No. 11. Those arguments pertinent to the grounds of rejection made and/or maintained in the instant office action are addressed herein. This action is not final.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 40 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The application discloses HSV-1 strain 1802 that is encompassed by the definitions for **biological material** set forth in 37 C.F.R. § 1.801. Because it is apparent that this biological material is essential for practicing the claimed invention, it must be obtainable by a reproducible method set forth in the specification or otherwise be known and readily available to the public as detailed in 37 C.F.R. §§ 1.801 through 1.809.

It is unclear whether this biological material is known and readily available to the public or that the written instructions are sufficient to reproducibly construct this biological material from starting materials known and readily available to the public. Accordingly, availability of such biological material is deemed necessary to satisfy the enablement provisions of 35 U.S.C. § 112. If this biological material is not obtainable or available, the requirements of 35 U.S.C. § 112 may be satisfied by a deposit of the biological material. In order for a deposit to meet all criteria set forth in 37 C.F.R. §§ 1.801-1.809, applicants or assignee must provide assurance of compliance with provisions of 37 C.F.R. §§ 1.801-1.809, in the form of a declaration or applicant's representative must provide a statement. The content of such a declaration or statement is suggested by the enclosed attachment. Because such deposit will not have been made prior to the effective filing date of the instant application, applicant is required to submit a verified statement from a person in a position to corroborate the fact, which states that the biological material which has been deposited is the biological material specifically identified in the application as filed (37 C.F.R. § 1.804). Such a statement need not be verified if the person is an agent or attorney registered to practice before the Office. Applicant is also reminded that the specification must contain reference to the deposit,

including deposit (accession) number, date of deposit, name and address of the depository, and the complete taxonomic description.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 44-47, 53-54 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 44 is vague and indefinite in that the metes and bounds of the term "stably integrated" are unclear. **This rejection is maintained for reasons of record in Paper No. 11 and repeated here.** This term does not appear to the clearly described in the specification. Under what conditions and for how long does the integrant have to be "stable"? How "stable" does the integrant have to be in order to satisfy the limitation? Does the limitation mean the integrant can never be removed from the viral genome by any means? It would be remedial to amend the claim language to more clearly indicate what is meant by a "stable" integrant.

Claims 53-54 provide for the use of replicatable recombinant herpesvirus, but, since the claim does not set forth any steps involved in the method/process as to their "use", it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Response to Arguments/112 2nd Paragraph

Applicant's arguments filed in the papers filed have been fully considered but they are not persuasive. The response essentially argues the term "stably integrated" is a term of art that is readily understood by the skilled artisan (e.g. the integrated DNA comprising the transgene will not be readily lost upon serial viral passage of the hybrid HSV/AAV strain). The response also argues that the specification provides a detailed description regarding genetic stability (e.g. page 6, lines 18-32). The assertion that the art recognizes the term "stably integrated" to have a particular meaning is unsupported and does not adequately address the specific questions raised in making the rejection. With regard to the teachings of the instant specification, the specification teaches "preferred" durations for which there is no "visible reversion", but does not provide a concrete figure or explicitly define "visible reversion". Therefore, the metes and bounds of the term "stably integrated" remain vague and indefinite.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 53-54 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 32-39, 41-60 are rejected under 35 U.S.C. 102(b) as being anticipated by Dong et al (WO 95/06743; reference AG on IDS #5 submitted by applicant; see the entire reference). **This rejection is maintained for reasons of record in the office action mailed 11/22/2002 and repeated below.**

Dong et al teach the construction of helper viruses for production of rAAV which comprise genes essential for AAV replication (e.g. Abstract). Dong et al teach that the helper viruses of their invention can be obtained from adenovirus or one of several different types of viruses classified in a general class of "herpesvirus", including HSV (e.g. page 6, lines 16-28). Dong et al teach that these helper viruses can either be replication competent (i.e. comprising viral packaging and origin of replication sequences) or replication defective (e.g. page 15, lines 19-29). Dong et al specifically teach that the herpesvirus helper viruses of their invention will, generally speaking, comprise one or more of the AAV rep, lip and cap genes (e.g. page 7, lines 8-20). Dong et al teach that the essential or non-essential genes from the helper virus genome have been deleted (e.g. page 7, lines 21-32). Dong et al teach that the helper viruses of their invention can promote expression of the essential AAV genes with either natural AAV promoters (e.g. p5 from AAV) or heterologous promoters (e.g. IE from CMV, retroviral

LTR elements) (page 8, lines 20-27; page 9, lines 4-14). The reference teaches that the nature of the herpes family virus is not believed to be crucial to the successful practice of the invention (e.g. herpes simplex virus, cytomegalovirus, etc.) (page 32, line 20 to page 33, line 9). Dong et al teach a prophetic example for insertion of AAV rep, lip and/or cap sequences into the genome of HSV feature the HSV vector R7020. R7020 features deletion of approximately 700 bp from the domain of the thymidine kinase gene and all of the sequences from the 3' end of the lE63 gene (a27) to the a4 gene in the reiterated sequences of the S component of the HSV genome. Dong et al teach that the rep-lip-cap sequences can be inserted in, at least, either of two positions including the site between the inserted tk gene and the HSV-2 DNA sequences and the site of the deletion of the natural tk gene (e.g. Example VI(1), page 44).

Response to Arguments

Applicant's arguments filed 11/22/2002 have been fully considered but they are not persuasive. The response essentially argues: 1) the Dong et al reference only discloses examples of recombinant adenovirus and does not reduce to practice the claimed invention, 2) Dong et al point to two papers published in 1980 which describe for the first time homologous recombination in the HSV genome and were fifteen years old at the time of filing of the Dong et al application, 3) the present application makes clear there were considerable obstacles to overcome before the presently claimed invention could be achieved, and therefore absent some demonstration that the contemplated viruses are genetically stable, that the transgenes are expressed at an acceptable level with the required regulation and that the desired packing of AAV vector DNA occurs, both the Dong references and the 1980 references upon which it relies cannot be considered as

enabling, 4) the present application indicates previous attempts at a system for replicating and packaging AAVs using herpesvirus amplicons met with failure due to the loss of the amplicons after only a few passages (e.g. page 4, lines 18-30; pages 3-4), and 5) Dong et al cannot be considered as enabling or as adequately describing the claimed modified recombinant herpesvirus, and therefore, cannot anticipate the claimed invention.

Dong et al is not required to reduce the invention to practice in order to be considered enabling. Dong et al clearly describe a recombinant HSV/AAV virus comprising the AAV rep and cap genes and its structural/functional requirements. With regard to the supposed inadequacies of the references upon Dong et al relies for its teachings concerning HSV, two points are relevant: 1) the age of the references is irrelevant to the claimed invention so long as what they teach is valid, and 2) it is not whether or not Dong et al was enabling at the time of filing of the Dong et al application, but whether the Dong et al reference would have been enabling at the time of the invention for the instant application. It is the examiner's contention that Dong et al were clearly enabling for the claimed invention at least at the time of filing of the instant application. With regard to arguments concerning the genetic stability of the inserted AAV sequences, expression of the transgene and desired packing of AAV DNA, these arguments appear to be directed to limitations that are absent in the rejected claims (e.g. the term "stably integrated" is not clearly defined and thus can be read broadly to encompass any degree of integration).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald G Leffers Jr., PhD whose telephone number is (571) 272-0772. The examiner can normally be reached on 9:30am-6:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

GERRY LEFFERS
PRIMARY EXAMINER

Gerald G Leffers Jr., PhD
Primary Examiner
Art Unit 1636

Ggl

SUGGESTION FOR DEPOSIT OF BIOLOGICAL MATERIAL
ATTACHMENT

A declaration by applicant or assignee, or a statement by applicant's agent identifying a deposit of biological material and averring the following may be sufficient to overcome an objection or rejection based on a lack of availability of biological material. Such a declaration:

1. Identifies declarant.

2. States that a deposit of the material has been made in a depository affording permanence of the deposit and ready accessibility thereto by the public if a patent is granted. The depository is to be identified by name and address. (See 37 C.F.R. § 1.803).

3. States that the deposited material has been accorded a specific (recited) accession number.

4. States that all restrictions on the availability to the public of the material so deposited will be irrevocably removed upon the granting of the patent. (See 37 C.F.R. § 1.808(a)(2)).

5. States that the material has been deposited under conditions that assure that access to the material will be available during the pendency of the patent application to one determined by the Commissioner to be entitled thereto under 37 C.F.R. § 1.14 and 35 U.S.C. § 122. (See 37 C.F.R. § 1.808(a)(1)).

6. States that the deposited material will be maintained with all the care necessary to keep it viable and uncontaminated for a period of at least five years after the most recent request for the furnishing of a sample of the deposited microorganism, and in any case, for a period of at least thirty (30) years after the date of deposit or for the enforceable life of the patent, whichever period is longer. See 37 C.F.R. § 1.806).

7. That he/she declares further that all statements made therein of his/her own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements were made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the instant patent application or any patent issuing thereon.

Alternatively, it may be averred that deposited material has been accepted for deposit under the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure (e.g., see 961 OG 21, 1977) and that all restrictions on the availability to the public of the material so deposited will be irrevocably removed upon the granting of a patent.

Additionally, the deposit must be referred to in the body of the specification and be identified by deposit (accession) number, date of deposit, name and address of the depository, and the complete taxonomic description.